TECHNICAL REPORT

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Outcome of the consultation with Member States and EFSA on the basic substance application for *Vitis vinifera* cane tannins for use in plant protection as fungicide on grapevine

European Food Safety Authority (EFSA)

Abstract

The European Food Safety Authority (EFSA) was asked by the European Commission to provide scientific assistance with respect to the evaluation of applications received by the European Commission concerning basic substances. In this context, EFSA's scientific views on the specific points raised during the commenting phase conducted with Member States and EFSA on the basic substance application for *Vitis vinifera* cane tannins are presented. The context of the evaluation was that required by the European Commission in accordance with Article 23 of Regulation (EC) No 1107/2009 following the submission of an application for approval of *Vitis vinifera* cane tannins as a basic substance for use in plant protection against mildew on grapevine. The current report summarises the outcome of the consultation process organised by EFSA and presents EFSA's scientific views on the individual comments received.

Keywords: *Vitis vinifera* cane tannins, basic substance, application, consultation, plant protection, pesticide

Requestor: European Commission

Question number: EFSA-Q-2018-00081

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Summary

Vitis vinifera cane tannins is an active substance for which, in accordance with Article 23(3) of Regulation (EC) No 1107/2009, the European Commission received an application from Biomolécules et Biotechnologies Végétales (BBV) EA2106 and Institut Technique de l'Agriculture Biologique, for approval as a 'basic substance'. Regulation (EC) No 1107/2009 introduced the new category of 'basic substances', which are described, among others, as active substances, not predominantly used as plant protection products but which may be of value for plant protection and for which the economic interest in applying for approval may be limited. Article 23 of Regulation (EC) No 1107/2009 lays down specific provisions for consideration of applications for approval of basic substances.

In March 2013, the European Commission requested the European Food Safety Authority (EFSA) to provide scientific assistance with respect to the evaluation of applications received by the European Commission concerning basic substances. By a further specific request, received from the European Commission in February 2018, EFSA was asked to organise a consultation on the basic substance application for *Vitis vinifera* cane tannins, to consult the applicant on the comments received, and to deliver its scientific views on the specific points raised in the format of a reporting table within three months of acceptance of the specific request.

A consultation on the basic substance application for *Vitis vinifera* cane tannins, organised by EFSA, was conducted with Member States via a written procedure in September-November 2017. Subsequently, EFSA also provided comments and the applicant was invited to address all the comments received in the format of a reporting table and to provide an application update as appropriate, within a period of 30 days.

The current report summarises the outcome of the consultation process organised by EFSA on the basic substance application for *Vitis vinifera* cane tannins and presents EFSA's scientific views on the individual comments received in the format of a reporting table.

Vitis vinifera cane tannins are extracted from crushed grape cane with ethanol. It is a complex mixture of stilbenoids (e.g. *E*-resveratrol, *E*-ε-viniferin, *E*-piceatannol, hopeaphenol) and flavonoids (e.g. catechin and epicatechin). Composition of active components may vary depending on grape cultivars. Applicant stated that the product should comply with International Oenological Codex, however according to the Codex, the Oenological Tannins are described as tannins extracted from grape seeds and not cane.

The intended use as a basic substance is as a fungicide in grapevine against downy mildew.

The toxicological assessment focuses on the reported main component *trans*-resveratrol, reviewed by the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) as a novel food ingredient in food supplements (EFSA NDA Panel, 2016); the toxicological profile of other biologically active components has not been addressed. Regarding *trans*-resveratrol, it is noted that it may be placed on the market as a novel food ingredient in food supplements intended for adult population only (with a maximum dose of 150 mg per day), and with specific labelling requirements that people using medicines should only consume the product under medical supervision (Commission Implementing Decision (EU) 2016/1190). Accordingly, a toxicological assessment should be performed for the substance used as plant protection products to ensure the protection of the whole population, including the more sensitive ones, such as children. This requirement would apply to estimate non-dietary exposure risk assessment, in particular bystanders and residents.

Satisfactory information addressing consumer exposure arising from the requested use of *Vitis vinifera* cane tannins as plant protection product was not submitted by the applicant. However, in view of the requested GAP with application to grape vines up to a latest growth stage of BBCH 57, i.e. before flowering, EFSA concluded unlikely that consumers of grape berries might be exposed to any significant amounts of biologically active components stemming from the application of the requested product. The relevance of consumer intakes related to residues on vine leaves, a commodity of minor importance in the EU diets, could not be assessed.

Satisfactory information demonstrating that grape canes are crushed and scattered in vineyards or composted for such further use and that this is reasonable wide scale practice that has been followed

for many years, as proposed by the applicant, was not available in the supporting publications provided. One of these supporting publications confirmed that the common practice was to burn the grape canes. Their experiment was to investigate the utility of composting grape canes to encourage it as a novel practice.

Insufficient information was available to perform risk assessments for birds, mammals, aquatic organisms and non-target arthropods. Therefore data gaps were identified. For the risk to bees and earthworms, data were available which may be useful to demonstrate a low risk, however, it was not demonstrated that the material used in the studies is sufficiently comparable to *Vitis vinifera* cane tannins. Therefore further data gaps were identified.

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

Regulation (EC) No 1107/2009[1] (hereinafter referred to as 'the Regulation') introduced the new category of 'basic substances', which are described, among others, as active substances, not predominantly used as plant protection products but which may be of value for plant protection and for which the economic interest of applying for approval may be limited. Article 23 of the Regulation lays down specific provisions to identify a substance as a basic substance with a view to ensure that such active substances that do not have an immediate or delayed harmful effect on human and animal health nor an unacceptable effect on the environment can be approved as 'basic' and used for plant protection purposes.

Vitis vinifera cane tannins is an active substance for which, in accordance with Article 23(3) of the Regulation, the European Commission received an application from Biomolécules et Biotechnologies Végétales (BBV) EA2106 and Institut Technique de l'Agriculture Biologique, for approval as a 'basic substance' for use in plant protection as against mildew on grapevine.

The European Food Safety Authority (EFSA) organised a consultation with Member States on the basic substance application for *Vitis vinifera* cane tannins, which was conducted via a written procedure in September-November 2017. The comments received, including EFSA's comments, were consolidated by EFSA in the format of a reporting table. Subsequently, the applicant was invited to address the comments in column 4 of the reporting table and to provide an application update as appropriate. The comments received and the response of the applicant thereon, together with the application update submitted by the applicant, were considered by EFSA in column 5 of the reporting table.

The current report aims to summarise the outcome of the consultation process organised by EFSA on the basic substance application for *Vitis vinifera* cane tannins and to present EFSA's scientific views on the individual comments received in the format of a reporting table.

The application and, where relevant, any update thereof submitted by the applicant for approval of *Vitis vinifera* cane tannins as a 'basic substance' in the context of Article 23 of the Regulation, is a key supporting documentation, therefore it is considered as a background documentation to this report and will also be made publicly available, excluding its appendices (Biomolécules et Biotechnologies Végétales, 2017, 2018).

1.2. Interpretation of the Terms of Reference

On 6 March 2013 the European Commission requested EFSA to provide scientific assistance with respect to the evaluation of applications received by the European Commission concerning basic substances. By a further specific request, received by EFSA on 2 February 2018, EFSA was asked to organise a consultation on the basic substance application for *Vitis vinifera* cane tannins, to consult the applicant on the comments received, and to deliver its scientific views on the specific points raised in the format of a reporting table.

To this end, a technical report containing the finalised reporting table is being prepared by EFSA. The agreed deadline for providing the finalised report is 2 May 2018.

On the basis of the reporting table, the European Commission may decide to further consult EFSA to conduct a full or focussed peer review and to provide its conclusions on certain specific points.

[1] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1-50.

2. Assessment

The comments received on the basic substance application for *Vitis vinifera* cane tannins and the conclusions drawn by EFSA are presented in the format of a reporting table.

The comments received are summarised in columns 2 and 3 of the reporting table. The applicant's considerations of the comments, where available, are provided in column 4, while EFSA's scientific views and conclusions are outlined in column 5 of the table.

The finalised reporting table is provided in Appendix A of this report. In addition, an overview table on the identity and biological properties of the substance and the list of intended uses in plant protection (GAP table) are provided in Appendix C and D, respectively.

Documentation provided to EFSA

1. Biomolécules et Biotechnologies Végétales, 2017. Basic substance application on *Vitis vinifera* cane tannins submitted in the context of Article 23 of Regulation (EC) No 1107/2009. June, 2017. Documentation made available to EFSA by the European Commission.

2. Biomolécules et Biotechnologies Végétales, 2018. Basic substance application update on *Vitis vinifera* cane tannins submitted in the context of Article 23 of Regulation (EC) No 1107/2009. January, 2018. Documentation made available to EFSA by the applicant.

References

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2016. Scientific opinion on the safety of synthetic trans-resveratrol as a novel food pursuant to Regulation (EC) No 258/97. EFSA Journal 2016;14(1):4368, 30 pp. doi:10.2903/j.efsa.2016.4368

European Commission, 2014. Guidance document on the procedure for application of basic substances to be approved in compliance with Article 23 of Regulation (EC) No 1107/2009. SANCO/10363/2012 rev.9, 21 March 2014.

OIV (Organisation Internationale de la Vigne et du Vin), 2015. International oenological codex oenological tannins COEI-1-tannins, INS N°: 181, (Oeno 12/2002 modified by Oeno 5/2008, 6/2008 and OIV-Oeno 352-2009) OIV-OENO 554-2015. 1–25.

Abbreviations

ADI	acceptable daily intake
a.s.	active substance
GAP	good agricultural practice
HPLC	High Performance Liquid Chromatography
LOAEL	lowest observable adverse effect level
MS	Member State
NOAEL	no observed adverse effect level

Appendix A – Collation of comments from Member States and EFSA on the basic substance application for Vitis vinifera cane tannins and the conclusions drawn by EFSA on the specific points raised

1. Purpose of the application

General					
No.	**Column 1** **Reference to application template**	**Column 2** **Comments from Member States/EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow-up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
	Overall	DK: Please delete template text (blue). If the applicant's tables and text is not self-explanatory without the template text, then please add some text; the template is somewhat esoterically filled out, including the use of references.		Removed in updated version	Addressed.

2. Identity of the substance/product as available on the market and predominant use

2.1. Identity and Physical and chemical properties of the substance and product to be used

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
2(1)	2.1.4 Method of manufacture, p.9	EFSA: A basic substance cannot be linked to a certain product, in this case Vinetan (or Vineatrol 30), which is a result of a manufacturing process.	The concept of basic substance would mean that the user can prepare the extract from the canes of *Vitis vinifera* spp., but for this there is a need of indicating the amounts of raw material and extraction solvents, extraction conditions,	Most of approved basic substances are a result of a manufacturing process. Nobody is able to access to fructose, sugar, whey, Beer, sunflower oil, lecithin, salix cortex, mustard seed powder... by themselves at home with raw plant material. Nobody knows all the extract process for these basic substances, including preservatives, anti-agglomerating, colouring or additive substances added. The process flowchart is presented in figure 2.1.4. Consequently anybody can reproduce the extraction process	Addressed. Vinetan is an example of product name as available on the market, however it will be mentioned that there are no data available concerning how the extraction should be done in practice.
2(2)	2. Identity of the substance, p.5	EFSA: the statement saying that *trans*-resveratrol is the main component is misleading and also the reference to a novel food ingredient, as the EFSA document is about	Is there any information about the content of *trans*-resveratrol of the extract to confirm this statement?	*trans*-resveratrol is the main known active component for plant protection: no misleading. However, all polyphenols also	Data gap. There aren't data to support the statement that *trans*-resveratrol is the main component.

2.1. Identity and Physical and chemical properties of the substance and product to be used					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
		safety of synthetic *trans*-resveratrol as a novel food pursuant to Regulation (EC) No 258/97[2], while this extract contains quite a number of other compounds, too.		contained may exhibit antioxidant properties useful for plant protection. The all substance exhibit fully described oenological grade specification.	The article submitted in the bibliography, for example Lambert et al. 'Comparative analyses of stilbenoids in canes of major *Vitis vinifera* L. cultivars' shows that at least three other stilbenoids are present at even higher levels than *E*-resveratrol.
2(3)	2.1.3.1 Tannins, p. 7	EFSA: tannins are also stated to be the major component, is it known which tannins are found in the extract?	In the bibliography reference is made to COMMISSION IMPLEMENTING REGULATION (EU) 2017/307[3] of 21 February 2017 concerning the authorisation of dry grape extract of *Vitis vinifera* spp. *vinifera* as a feed additive for all animal species except for dogs. In the annex of this regulation there is a kind of specification of the product with the respective analytical methods. Something similar would be helpful also in this case.	The substance exhibit fully described oenological grade specification (International oenological CODEX).	According to International oenological CODEX on oenological tannins (OIV, 2009) oenological tannins are extracted from nutgalls, or a wood rich in tannin: chestnut trees, oak, exotic wood, or grape **seeds**. Grape tannins are formed from 3-flavonol units, which can be released by thiolytic cleavage of the flavonol intermonomer linkages in proanthocyanidols under heat in an acid medium. The

[2] Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients. OJ L 43, 14.2.1997, p. 1–6.
[3] Commission Implementing Regulation (EU) 2017/307 of 21 February 2017 concerning the authorisation of dry grape extract of *Vitis* vinifera spp. vinifera as a feed additive for all animal species except for dogs. OJ L 44, 22.2.2017, p. 1–5.

2.1. Identity and Physical and chemical properties of the substance and product to be used					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
					monomers thus released are then separated and assayed using HPLC. This means that the procyanidols and prodelphinidols can be quantified separately. This method is used to identify tannins from grape skins, stems and seeds. Based on International oenological CODEX (OIV, 2009) a kind of specification might be: total flavanol content expressed as (+) catechin min. 50 mg/g or proanthocyanic tannin content min. 0.5 mg/g. It has however to be noted that *Vitis vinifera* cane tannins are extracted from crushed grape cane with ethanol.
2(4)	2.1.3.2 Resveratrol, p. 7	EFSA: if *trans*-resveratrol is considered the main active component, are there any information available on the		Composition % updated in the basic substance application. Cultivar variations introduced:	Addressed: Concentrations of stilbenoids in woody canes of 16 *Vitis vinifera* L. cultivars were

2.1. Identity and Physical and chemical properties of the substance and product to be used					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
		content of this compound originating from any variety of *Vitis vinifera* spp. throughout Europe		Lambert et al 2013 J. *Agric. Food Chem.* 61(47), 11392-11399 Guerrero, 2016 References added	presented in Lambert et al, 2013
2(5)	2.1.3.2 ε-viniferin, p. 8	EFSA: it seems that there are other active components, too like δ-viniferin and pterostilbene which are active against *Plasmopara viticola*		Polyphenols are indeed suspected to be active in the extract because their antioxidant properties. Pterostilbene and δ-viniferin are not present in canes	Addressed.
2(6)	2.1.5 Specification of purity of the a.s., p.9	EFSA: if the *Vitis vinfera* cane extract is considered the active substance, but the activity is linked to certain components of the extract, it would be helpful to have a kind of specification, a minimum content of those components assuring the efficacy of the product		Specifications are clearly described as Oenological 'tannins' grade certification (CODEX). Composition % updated in the basic substance application	Addressed. The basic substance should comply with the International Oenological Codex (OIV, 2009). The specification was updated in the updated application.
2(7)	2.1.7 Method of analysis, p.10	EFSA: this table containing the min. content of *trans*-resveratrol, *trans*-ε-viniferin and total resveratrol monomers and oligomers is considered a kind of specification of the product?		Specifications and Method of analysis are specified by CODEX. Composition % updated in the basic substance application	Addressed. See also comments 2(6) and 2(3)

2.2. Current Former and in case proposed trade names					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
2(8)		DK: It is stated that VineTan is the commercially available substance, and that VINEATROL 30 is not sold for this purpose. Does that indicate that VineTan is sold for this purpose?!	DK: Please explicitly state for what purpose each of the listed trade names is placed on the market.	Corrected in the updated basic substance application Vintan exhibits Oenological 'tannins' grade certification (CODEX) and sold for that purpose.	Addressed. See also comment 2(1)

2.3. Manufacturer of the substance/products					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**

2.4. Type of preparation					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**

2.5. Description of the recipe for the product to be used					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
2(1)	2.5 Description of the recipe, p.11	EFSA: it is not clear if the 8 g/l final concentration means 8 g of *Vitis vinifera* extract, or 8 g of product (Vineatrol 30)?		8 g/L is the concentration of *Vitis vinifera* oenological tannin (i.e. Vinetan)	Addressed.

3. Uses of the substance and its product

3.1. Field of use

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application

No comments

3.2. Effects on harmful organisms or on plants

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
3(1)	3.2.1 Effects on harmful organisms	DK: Please link this section to the GAP.	DK: Please justify the application rates etc. in the GAP based on references and/or trials included in this section.	Trials are cited in §3 IFV 2016 **&** Lanoue 2016. GAPs are defined corresponding to these trials. Gabaston et al 2018 J Pest Sci,	Addressed.
3(2)	3.2.2 Mode of action, p. 13	EFSA: it is not clear how the stilbene-enriched extracts are obtained. Is this something different from the a.s. in discussion or just a different way of expressing the same thing?		Stilbene-enriched extracts are the oenological grade tannins. Extraction is described in §2. Mode of action (MOA) is updated in the basic substance application.	Addressed.

3.3. Summary of intended uses					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
3(3)	3.4 Summary of intended uses	DK: Please use a dot (.) and not commas (,) to separate decimals on the GAP as the application is in English.	DK: Update GAP.	Corrected in the updated basic substance application	Addressed.

4. Classification and labelling of the substance

Classification and labelling of the substance					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**

No comments

5. Impact on Human and Animal Health

5.1. Toxicokinetics and metabolism in humans

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application

No comments

5.2. Acute toxicity

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application

No comments

5.3. Short-term toxicity

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA		Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
5(1)	"Trials were done in 2001".	DE: Resveratrol is a phytoestrogen acting as	A literature review on the (phyto)estrogenic and other	EFSA already approved *trans*-Resveratrol (synthetic as feed	The EFSA NDA panel has reviewed the oestrogen

5.3. Short-term toxicity

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA		Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
		mixed estrogen receptor agonist/antagonist – see for example Bowers et al. (2000) Endocrinology 141:3657–3667. doi: 10.1210/endo.141.10.7721. Furthermore, it has been suggested that an antiandrogenic effect of resveratrol is based on inhibition of 3-beta-hydroxysteroiddehydrogenase in Leydig cells (Li et al., (2014) Toxicol Lett. 2014 Apr 7;226(1):14-9. doi: 10.1016/j.toxlet.2014.01.022.) In mice testes, Leydig cell toxicity and degeneration of seminiferous tubules was reported (Ranawal et al., (2014) Andrologia. 2014 Aug;46(6):650-8. doi: 10.1111/and.12132). Finally, 25 mg/kg bw/d was reported to induce thyroid cell proliferation, thyroid size and TSH levels in rats through Na/I symporter	endocrine activities as well as a critical discussion of the potential implications for human and animal health should be included. Available toxicity studies should be carefully evaluated with regard to effects on the thyroid and organs under androgen/estrogen control.	and food), consequently we found these comment quite surprising for resveratrol as basic substance application. These points have been already ruled during approval of resveratrol as feed additive. See in 2016 in whereas 4 of Implementig Reg. (UE) 2017/307 "under the proposed conditions of use in feed, the substance concerned does not have adverse effect on animal health, human health or the environment." See also EFSA NDA Panel, 2016. Both references belong to EFSA and they are subsequent to the cited references (2014).	effects reported in the literature and considered that these data do not indicate concerns with respect to oestrogenic activity of resveratrol *in vivo*. However the panel considered that studies in humans per se did not provide sufficient evidence of safety. Considering the weight of evidence, the Panel concluded that the intended intake level of 150 mg/day for adults does not raise safety concerns. Accordingly, a toxicological assessment should be performed for the substance used as plant protection products to ensure the protection of the whole population, including the more sensitive ones, such as children. See also comments 5(7), 5(9) and 5(10)

5.3. Short-term toxicity

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA		Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
		inhibition of iodine uptake into thyrocytes (Giuliani at al. (2017) Food Chem Toxicol. 2017 Sep;107(Pt A):237-247. doi: 10.1016/j.fct.2017.06.044.)			
5(2)	"Trials were done in 2001".	DE: Studies cited refer to acute toxicity but not short-term toxicity.	The 28-day study referenced in chapter 5.5 should be described in detail in 5.3.	Reference Bio HC 2001d moved to §5.2 These points have been already ruled during approval of resveratrol as feed additive.	Addressed.
5(3)	"Trials were done in 2001".	DK: Agree with DE comment.		Reference Bio HC 2001d moved to §5.2	Noted. See comment 5(2)
5(4)	"Trials were done in 2001".	DK: Agree with DE comment.		Reference Bio HC 2001d moved to §5.2	Noted. See comment 5(2)

5.4. Genotoxicity

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application

No comments

5.5. Long-term toxicity

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
5(5)	„Trials were done in 2009".	DE: The 28 day study cited is not a long-term study but short-term (chapter 5.3).	Please add data on long-term toxicity and carcinogenicity.	Reference Intox 2009 moved to §5.3	Addressed.
5(6)	„Trials were done in 2009".	DK: Agree with DE comment.		Reference Intox 2009 moved to §5.3	Noted. See comment 5(5)

5.6. Reproductive toxicity

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
5(7)	'No negative data'	DE: Adverse effects on testes and androgen synthesis are reported in the literature. Please refer to comment on chapter 5.3 relating to		Reference Bio HC 2001d moved to §5.2 These points have been already ruled during approval	See comment 5(1)

5.6. Reproductive toxicity

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
		effects on estrogen/androgen and thyroid system.		of resveratrol as feed additive. See EFSA NDA Panel, 2016	
5(8)	'No negative data'	DK: Agree with DE comment.			Noted. See comment 5(7)

5.7. Neurotoxicity

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 4 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application

No comments

5.8. Toxicity studies on metabolites

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application

No comments

5.9. Medical Data: adverse effects reported in humans					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**

No comments

5.10. Additional Information related to therapeutic properties or health claims					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**

No comments

5.11. Additional information related to use as food					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
5(9)	5. Use of *trans*-resveratrol as novel food, p. 19	EFSA: According to the Commission Implementing Decision (EU) 2016/1190[4], *trans*-resveratrol may be placed on the market as a novel food ingredient in food supplements intended for adult population only (with a		Resveratrol is sold as food supplements without medical supervisioni.e. arkopharma ;granions; pileje, ponroy, caudalie… with content up to 470 mg / pills. Basic substance application bibliography §2 updated	See comment 5(1)

[4] Commission Implementing Decision (EU) 2016/1190 of 19 July 2016 authorising the placing on the market of trans-resveratrol as a novel food ingredient under Regulation (EC)No 258/97 of the European Parliament and of the Council (notified under document C(2016) 4567) OJ L196 of 21.7.2016 pp. 53-55

5.11. Additional information related to use as food					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
		maximum dose of 150 mg per day), and labelling of the food supplements containing *trans*-resveratrol shall bear a statement that people using medicines should only consume the product under medical supervision. These requirements are not compatible with the use of the substance as a plant protection product.			

5.12. Acceptable daily intake, acute reference dose, acceptable operator exposure level					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
5(10)	5.12 toxicological reference values, p. 22	EFSA: Given the uncertainties and lack of investigations of toxicological endpoints (long term, reproduction, and developmental toxicity) for resveratrol, a higher uncertainty factor of 1000	A revision of the proposal for toxicological reference values should be provided for *trans*-resveratrol and an assessment of the toxicological relevance of other components of *Vitis vinifera* cane tannins should	Exposure through dietary supplements is primarily oral, although one source provided information on a topical cream containing resveratrol. Recommended dosages for oral dietary supplements	See comment 5(1)

5.12. Acceptable daily intake, acute reference dose, acceptable operator exposure level

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
		could be used to derive the ADI from a 90-day toxicity study. It is unclear where the NOAEL of 750 mg/kg bw per day is established since the EFSA panel on dietetic products, nutrition and allergies (NDA) identified a LOAEL at 120 mg/kg bw per day (EFSA, 2016). The NDA panel established 150 mg/day as a level not raising safety concerns, but it is limited to adults risk assessment.	be provided.	range from 2.495 mg to 1 g (0.01091 µmol to 4 mmol). Ref added to updated basic substance application	

5.13. Impact on human and animal health arising from exposure to the substance or impurities contained in it

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
5(11)	2.1.3.1 Tannins: ε-viniferin, ACACIA SENEGAL GUM E414, p. 7	EFSA: the toxicological assessment focuses on the main component *trans*-resveratrol, however the full		Oenological tannin grade implies food CODEX specifications.	The toxicological profile of other biologically active components besides trans-resveratrol present in *vitis*

5.13. Impact on human and animal health arising from exposure to the substance or impurities contained in it					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
		composition of *Vitis vinifera* canes is not given and other compounds are present in significant levels (see EFSA comment 2(5)), but no toxicological data/assessment are available for the remaining components.		Other components like acacia Senegal gum exhibit food status (E414).	*vinifera* should also be determined.

6. Residues

Residues					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
6(1)		ESFA: An estimation of residues or any consumer exposure consideration was not submitted in the application. It is insufficient to conclude that residues are not of concern without substantiating this claim. Absence of dietary safety concerns established in a defined area of use (e.g. novel food) does not necessarily mean that uses in other areas resulting into dietary consumer exposure are automatically safe. A use specific assessment has to be conducted. Upon clarification of the main components in this basic substance application (see sections on identify/ description of product) and finalisation of the toxicological assessment of the components in this basic	Upon clarification of the main components apart from *trans*-resveratrol and ε-viniferin (resveratrol dimer), and upon finalisation of the toxicological assessment of all relevant components in this basic substance application, an assessment of the consumer exposure potential should be provided, taking into account also the latest possible application from the requested GAP, in order to complete the risk assessment.	Grape cane tannin is used as fertilizer (compost) with high quantities reintroduced in vineyards. References added in the updated basic substance application. Content of tannin is more described in the basic substance application. Resveratrol is food additive authorized. Tannins containing resveratrol and ε-viniferin are use in wine making as allowed oenological additive, thus residues have been evaluated as negligible or non-relevant for human consumption since tannins are already present in grape berries and also in red wines. *trans*-resveratrol (synthetic) is also approved as feed and food. Consumer is already	EFSA takes note of the applicant's response that does still not address the actual use pattern that is requested with this application. As for the hazard assessment of the compounds contained in the grape cane extracts (not only resveratrol but also resveratrol dimers, tetramers, catechin and its derivatives and other compounds) it is referred to the section Impact on Human and Animal Health (toxicology). Again, if residues "have been evaluated as negligible or non-relevant" in assessment areas other than pesticides, it is still necessary to provide a consumer exposure assessment that is relevant to the requested use as plant protection product, which the applicant has not fulfilled.

Residues					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
		substance application, further consideration on the consumer exposure and consumer safety should be made. The time of last application is also an important criterium to assess the likelyhood of residues to which consumers could be exposed to.		exposed to beneficial activity of tannins.	However, in view of the requested GAP for the use of grape vine cane extract to grape vines up to a latest growth stage of BBCH 57 (before flowering) EFSA can conclude that it is unlikely that consumers of grape berries might be exposed to any significant amount of residues of possibly biologically active components stemming from a GAP-conform use of the proposed product. The scenario of consumption of treated young vine leaves was not assessed. Public literature suggests that distribution of resveratrol in grape is organ-specific and tissue-specific and that stem phloems present the most abundant amounts of resveratrol, while the leaves presented the lowest. Hence, an enrichment of concentrations of resveratrol

Residues					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
					on treated leaves above concentrations naturally present in vine leaves cannot be excluded; however as nothing is known on degradation behavior and magnitude of such residues it is currently unknown whether these levels may have any impact on the health of consumers of vine leaves.

7. Fate and Behaviour in the environment

7.1 Fate and Behaviour in the environment					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
7(1)		ES: No data is submitted in the fate and behaviour section. However, as specified by the applicant grape wastes are generally reintroduced in vineyards as organic fertilizer (compost). Grape		Compost/fertilizing uses added. Compost from grape is reintroduced in vineyards up to 500 kg/ha. More references added in the updated basic substance	See comment 7(2).

7.1 Fate and Behaviour in the environment

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
		canes are crushed and scattered in vineyards and nature (as fertilizer) or composted for such further use According to page 13 of European Commission, 2014: 'Based on the description of the intended uses, the potential consequences of increased exposure with respect to natural exposure levels of water, soil or air or to exposure due to other uses should be considered and substantiate that the substance will not have "an unacceptable effect on the environment'. May applicant submit information on this point?		application.	
7(2)		EFSA: Some papers have been provided indicating that grape must may be composted and reintroduced as a fertiliser in vineyards.	EFSA: Please provide evidence of reasonable wide scale practice for: Grape canes being crushed and scattered in vineyards and nature (as	Compost/fertilizing uses added. Compost from grape is reintroduced in vineyards up to 500 kg/ha.	Satisfactory information supporting the statement that 'Grape canes are crushed and scattered in vineyards ……. or composted for such further

7.1 Fate and Behaviour in the environment					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
		However comparable evidence was not provided to support the statement that 'Grape canes are crushed and scattered in vineyards ……. or composted for such further use' Please provide evidence that this is reasonable wide scale practice. It seems improbable to the commenter that grape canes can be composted?	fertiliser) or composted for such further use.	More references added in the updated basic substance application.	use' and that this is reasonable wide scale practice was not available. The reference Nikolaidoua (2010) states that in Greece in both conventional and organic vineyards the common practice is to burn grape canes, not compost them. Nikolaidoua (2010) is an experiment investigating cutting and composting grape canes that demonstrates that this is a potential practice. Ferrer (2001) investigated adding chicken manure to vineyard waste whilst composting (not actually stated if this included grape canes). However both are academic investigation / experiments. It is not evidence that composting grape canes is / has been wide scale practice.

7.2 Estimation of the short and long-term exposure of relevant environmental media (soil, groundwater, surface water)					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**

8. Effects on non-target species

8.1. Effects on terrestrial vertebrates					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
8(1)	Introduction	DK: Please delete the statement, that no adverse effect is expected from the use due to the natural occurrence of the proposed basic substance. It is well know that many natural occurring compounds are toxic, therefore this statement can be read as misguided. Also, the application is for spraying with tannins, something that is not naturally occurring.		Sentence moved to mammal section. Grape cane tannins are usually used in vineyards as compost (grape canes) and in wine making process. Additionally, major compounds are already approved for all animals (except dogs), so it cannot be considered as toxic either for plants or animals.	Addressed.
8(2)	8.1	DK: Please include some kind of	Please update the application to	Major component is allowed	Data gap

8.1. Effects on terrestrial vertebrates

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
		risk assessment for birds and mammals. As is it is a (limited) collection of references to make indicate that the proposed basic substance has a low hazard to vertebrates when included in the diet. However, this says very little of the risk of the proposed use of the substance.	include a risk assessment for birds and mammals where the proposed use (spray application) has been included. Or at least link the safe dietary doses from literature to the expected dietary exposure from the proposed uses (acute and long-term).	for most animals and humans. Substance itself is present in grape berries, red wines, peanuts, chocolate.	A risk assessment considering the level of exposure expected for birds and mammals is needed. Furthermore, please note the data gap under point 2(2) of section 2.1 requesting further information of the composition of the active substance. It may be necessary to consider the risk to non-target organisms from components other than resveratrol.
8(3)	8.1.	EFSA: As requested by the comment from DK, the available information should be used in some form of risk assessment to demonstrate a low risk to birds. Furthermore, the relevance of the studies by Sahin et al., 2010, and Naumann Harley et al., 2013, to the risk assessment for wild birds and mammals should be explained.	EFSA: An explanation of the relevance of the assessments made in the available studies should be provided. The tested doses which were assessed should then be considered relative to that expected for the representative use.	These points have been already ruled during approval of resveratrol as feed additive. See EFSA NDA Panel, 2016 Other component like gum is food additive (E414).	Refer to data gap under comment 8(2).

8.2. Effects on aquatic organisms

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
8(4)		ES: Please refer to ES comment of fate section.			Noted.
8(5)	Ibid.	DE: The submitted study (Leiro et al., 2004) is not suitable to assess the risk for aquatic organisms of the intended uses.	DE: Provide a sound risk assessment for aquatic organisms.	More reference added in updated basic substance application on resveratrol uses for fish feed (Valenzano et al 2006; leiro et al., 2004; Xin et al., 2012). Resveratrol has positive impact on longevity.	Data gap Data and a risk assessment are needed to demonstrate a low risk to aquatic organisms. The risk assessment should cover the risk to fish, aquatic invertebrates and algae. Furthermore, please note the data gap under point 2(2) of section 2.1 requesting further information of the composition of the active substance. It may be necessary to consider the risk to non-target organisms from components other than resveratrol. The information summarised in the application only consider fish and are not considered to demonstrate a low risk.
8(6)		DK: Agree with DE comment; study is not appropriate for risk assessment.	DK: Please include an appropriate risk assessment for aquatic organisms.		Refer to data gap under comment 8(2).

8.2. Effects on aquatic organisms

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
8(7)	8.2	EFSA: The comments of DK and DE are agreed. The study of Leiro et al. (2004) is not suitable to derive relevant information for the risk assessment.	EFSA: Unless it is demonstrated that exposure to aquatic organisms is within background levels in water then reliable information is needed in order to perform a risk assessment for fish.	More reference added in updated BSA on resveratrol uses for fish feed. Resveratrol has positive impact on longevity.	Refer to data gap under comment 8(2).
8(8)	8.2	EFSA: No information has been provided to assess the risk to aquatic invertebrates and algae.	EFSA: Unless it is demonstrated that exposure to aquatic organisms is within background levels in water reliable information is needed in order to perform a risk assessment for aquatic invertebrates and algae.	Resveratrol is added to fish food.	Refer to data gap under comment 8(2).

8.3. Effects on bees and other arthropods species

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
8(9)	8.3.2 Effects on other arthropods	DE: The submitted study (CETU, 2015) showed a possible toxic effect on spider mites. The submitted data are not suitable to assess the risk of	DE: Provide a sound risk assessment for non-target arthropods.	Study said: "We can also notice that phytoseiids are more numerous on the AB plot than that conducted in reasoned. There is therefore	Data gap Data and a risk assessment are needed to demonstrate a low risk to non-target

8.3. Effects on bees and other arthropods species

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
		the intended uses to non-target arthropods. A risk assessment for this group of organisms is not possible.		no negative effect of shoot treatments on densities populations of phytoseiids." Or" There is therefore no negative effect of shoot treatments (4g / l and 8g / l) on population densities of phytoseiids and spider mites." Grape cane extract has no effect on earthworms (Gabaston et al 2018)	arthropods. The study by CETU (2015) indicates a potential effect on phytoseiids.
8(10)	8.3.2 Effects on other arthropods	DK: Agree with DE comment.	DK: Please include an appropriate risk assessment for non-target arthropods.		Refer to data gap under comment 8(9).
8(11)		DK: Please note that the GAP is for BBCH 10-57, therefore the risk to bees may be negligible.		No comment from applicant	Refer to data gap under comment 8(9).
8(12)	8.3.2 Effects on other arthropods	EFSA: The comment of DE and DK regarding the risk to non-target arthropods is agreed.		No comment from applicant	Refer to data gap under 8(9).
8(13)	8.3.1. Effects on bees	EFSA: The comment of DK is correct to highlight that the GAP does not include flowering stages of vines. However, to further support		Polyphenols in canes are similar to natural grape pollen. Indeed trans-resveratrol is present in certain amount.	Data gap Please note the data gap under point 2(2) of section 2.1 requesting further

8.3. Effects on bees and other arthropods species

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
		a low risk to bees from residues in pollen/nectar on the treated crop, it would be useful if information was available to support the assumption that there is no systemic translocation. Furthermore, exposure to bees can occur via several routes including residues in weeds in the treated crop and also in the field margin.		Polyphenols from treatment do not differ from grape polyphenol and are similar to those of pollen. Ares et al. (2015) more detailed in the basic substance application. Spray on pollinators is ll	information of the composition of the active substance. It may be necessary to consider the risk to non-target organisms from components other than resveratrol. With regard to the risk to bees from resveratrol, a low can be concluded. The summarised paper of Ares et al. 2015 does not provide any meaningful information to the risk assessment as it is discussing analytical techniques. However, Costa et al. (2009)[1] investigated the effects of using resveratrol as a treatment for nosema virus. It was found that the longevity of the bees was longer in the group treated with resveratrol (10 ppm). Although, the endpoint has not been used in a quantitative risk assessment, given that exposure to bees

8.3. Effects on bees and other arthropods species					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
					will only be via weeds, on balance a low risk to honeybees from resveratrol can be concluded. [1]Costa, C., Lodesani, M. & Maistrello, L. Apidologie (2010) 41: 141. https://doi.org/10.1051/apido/2009070
8(14)	8.3.1. Effects on bees	EFSA: The results of the study of Ares et al. (2015) have not been included in the application. However, consideration of the original study indicates that trans-resveratrol is detected in bee pollen. However, it should be considered whether the levels detected in bee pollen are relevant to that expected from the GAP under consideration.	EFSA: The study should be summarised in sufficient detail and the results included. The results of the study should also be considered in the context of the likely exposure expected from the GAP under consideration.	Conclusion of Ares et al. (2015) added in the BSA: trans-Resveratrol is contained in pollens collected from bees from 90–9100 µg/kg.	Refer to data gap under comment 8(13).

8.4. Effects on earthworms and other soil macroorganisms

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application
8(15)	8.4 Effects on earthworms and other soil macro-organisms	EFSA: The study of Nogales et al. (2005) should be summarised in more detail. However, consideration of the original study, the results indicate that the number of earthworms and the biomass of earthworms was less than the control group (manure) for the groups tested with spent grape marc, vinasse biosolids mixed with vine shoots and lees cake mixed with vine shoots. It is therefore not clear how the results of this study are considered to show a low risk to earthworms. Please provide further explanation.	EFSA: The study should be summarised in detail and the results considered in the context of risk assessment.	Conclusion of the publication: No mortality of earthworms was detected in any of the substrates during the 16-week experimental period. More ref added in updated basic substance application regarding grape extract safety vs earthworms.	Data gap The relevance of the test material used in the study of Gabaston et al. (2018) to *Vitis vinifera* cane tannins should be demonstrated. It would also be useful if the endpoint from the study was used in a quantitative risk assessment. The study of Nogales et al. (2005) is of limited use for risk assessment. However, a newly submitted study Gabaston et al. (2018) demonstrates that extract obtained from grapevine root did not cause mortality to earthworms. However, it is not clear how the composition of the tested extract compares to the composition of *Vitis vinifera* cane tannins.

No comments

8.5. Effects on soil microorganisms

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application

No comments

8.6. Effects on other non-target organisms (flora and fauna)

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application

No comments

8.7. Effects on biological methods of sewage treatment

No.	Column 1 Reference to Application Template	Column 2 Comments from Member States / EFSA	Column 3 Proposal by Member States/EFSA on how the application should be updated to address the comment	Column 4 Follow up response from applicant	Column 5 EFSA's scientific views on the specific points raised in the commenting phase conducted on the application

No comments

9. Overall conclusions with respect of eligibility of the substance to be approved as basic substance

Overall conclusions with respect of eligibility of the substance to be approved as basic substance					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
9(1)	(b) does not have an inherent capacity to cause endocrine disrupting, neurotoxic or immunotoxic effects;	DE: Resveratrol was identified as main component of the a.s. in chapter 2.1.3.2 with >30 % according to 2.1.7. and the assessment of the impact on human and animal health was based to a large extent on resveratrol. However, resveratrol is a phytosestrogen acting as mixed estrogen receptor agonist/antagonist – see for example Bowers et al. (2000) Endocrinology 141:3657–3667. doi: 10.1210/endo.141.10.7721. Accordingly, a more critical scientific discussion of the potential endocrine disruption properties should be included. Some authors did describe resveratrol as an endocrine disruptor (e.g. Ziolkowska et al. (2006) Int J Mol Med. 2006 Dec;18(6):1165-8.	A literature review on the (phyto)estrogenic activities and implications for human health should be performed and included in chapter 5.	EFSA mentioned *trans*-resveratrol (synthetic) has been already approved as feed and food. Now you mention toxicity of the same compound and you ask for toxicity studies for approved food and feed compound. These points have been already ruled during approval of resveratrol as feed additive. See in 2016 in whereas 4 of Impl. Reg. (UE) 2017/307 "under the proposed conditions of use in feed, the substance concerned does not have adverse effect on animal health, human health or the environment." See also EFSA NDA Panel, 2016 Both references belong to EFSA and they are subsequent to the cited references (2014).	See comment 5(1)

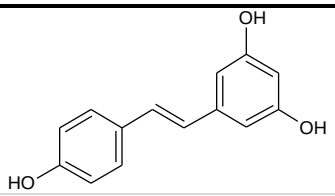
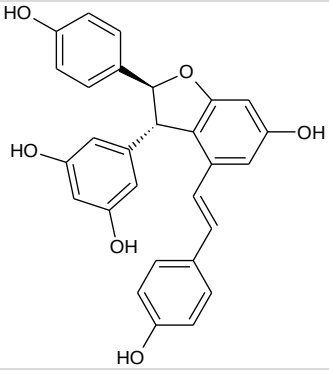
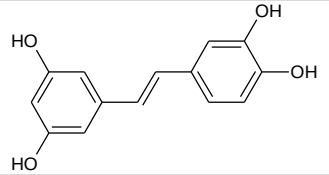
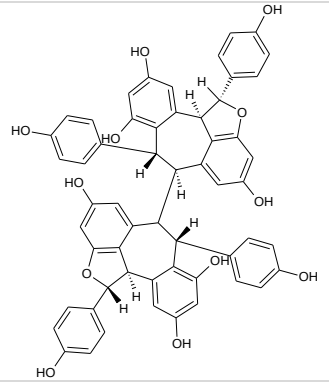
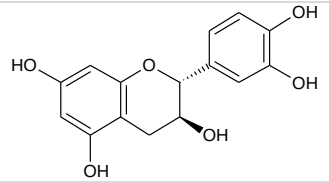
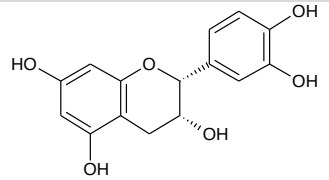
Overall conclusions with respect of eligibility of the substance to be approved as basic substance					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**
9(2)	(b) does not have an inherent capacity to cause endocrine disrupting, neurotoxic or immunotoxic effects;	DK: Agree with DE comment.		Substance and major active component are not a substance of concern: food and feed additive, evaluated by EFSA, CODEX.	See comment 5(1)

10. Other comments

Other comments					
No.	**Column 1** **Reference to Application Template**	**Column 2** **Comments from Member States / EFSA**	**Column 3** **Proposal by Member States/EFSA on how the application should be updated to address the comment**	**Column 4** **Follow up response from applicant**	**Column 5** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the application**

No comments

Appendix B – Used compound codes

Code/trivial name	IUPAC name/SMILES notation/InChiKey[a]	Structural formula[b]
***E*-resveratrol *trans*-resveratrol**	5-[(*E*)-2-(4-hydroxyphenyl)ethenyl]benzene-1,3-diol Oc2cc(/C=C/c1ccc(O)cc1)cc(O)c2 LUKBXSAWLPMMSZ-OWOJBTEDSA-N	
***E*-ε-viniferin**	5-{(2*S*,3*S*)-6-hydroxy-2-(4-hydroxyphenyl)-4-[(*E*)-2-(4-hydroxyphenyl)ethenyl]-2,3-dihydro-1-benzofuran-3-yl}benzene-1,3-diol Oc1ccc(cc1)/C=C/c2cc(O)cc3O[C@@H]([C@H](c23)c4cc(O)cc(O)c4)c5ccc(O)cc5 FQWLMRXWKZGLFI-BQYFGGCBSA-N	
***E*-piceatannol**	4-[(*E*)-2-(3,5-dihydroxyphenyl)ethenyl]benzene-1,2-diol Oc2ccc(/C=C/c1cc(O)cc(O)c1)cc2O CDRPUGZCRXZLFL-OWOJBTEDSA-N	
hopeaphenol	(1*R*,1'*R*,6*S*,7*R*,7'*R*,11b*R*,11b'*R*)-1,1',7,7'-tetrakis(4-hydroxyphenyl)-1,1',6,6',7,7',11b,11b'-octahydro[6,6'-bi-2-oxadibenzo[*cd*,*h*]azulene]-4,4',8,8',10,10'-hexol Oc1ccc(cc1)[C@@H]%12Oc2cc(O)cc5c2[C@H]%12c3cc(O)cc(O)c3[C@@H](c4ccc(O)cc4)C5[C@@H]%11c7cc(O)cc8O[C@@H](c6ccc(O)cc6)[C@@H](c78)c9cc(O)cc(O)c9[C@H]%11c%10ccc(O)cc%10 YQQUILZPDYJDQJ-KLIIVJQHSA-N	
catechin	(2*R*,3*S*)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2*H*-1-benzopyran-3,5,7-triol Oc1ccc(cc1O)[C@H]2Oc3cc(O)cc(O)c3C[C@@H]2O PFTAWBLQPZVEMU-DZGCQCFKSA-N	
epicatechin	(2*R*,3*R*)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2*H*-1-benzopyran-3,5,7-triol Oc1ccc(cc1O)[C@H]2Oc3cc(O)cc(O)c3C[C@H]2O PFTAWBLQPZVEMU-UKRRQHHQSA-N	

(a): ACD/Name 2015 ACD/Labs 2015 Release (File version N20E41, Build 75170, 19 Dec 2014)
(b): ACD/ChemSketch 2015 ACD/Labs 2015 Release (File version C10H41, Build 75059, 17 Dec 2014)

Appendix C – Identity and biological properties

Common name (ISO)	*Vitis vinifera* cane tannins (Not ISO)
Chemical name (IUPAC)	Not applicable (complex mixture)
Chemical name (CA)	Not applicable (complex mixture)
Common names	*Vitis vinifera* L. cane extract; *Vitis vinifera* L. extract
CAS No	84929-27-1
CIPAC No and EEC No	284-511-6 (EINECS/ELINCS)
FAO specification	none
Minimum purity	OENOLOGICAL TANNINS (INS N°: 181 (Oeno 12/2002 modified by Oeno 5/2008, 6/2008 and OIV-Oeno 352-2009) OIV-OENO 554-2015 1
Relevant impurities	OENOLOGICAL TANNINS (INS N°: 181 (Oeno 12/2002 modified by Oeno 5/2008, 6/2008 and OIV-Oeno 352-2009) OIV-OENO 554-2015 1 As max. 3 mg/kg Pb max 5 mg/kg Hg max. 1 mg/kg
Molecular mass and structural formula	Not applicable (complex mixture)
Mode of Use	spray
Preparation to be used	Dispersible powder (DP)
Function of plant protection	fungicide

Appendix D – List of uses

Crop and/or situation (a)	Member State or Country	Example product name as available on the market	FGI (b)	Pests or group of pest controlled (C)	Formulation		Application				Application rate per treatment			Total rate	PHI (days) (m)	Remarks
					Type (d-f)	Conc of a.i. g/L (i)	Method kind (f-h)	Growth stage and season (j)	Number min max (k) a) per use b) per crop/ season	Interval between applications (min)	kg a.i./hl min max (kg/hl	Water l/ha min max	kg a.i./ha min max (kg/ha) (l)	kg a.i./ha min max (kg/ha) (l)		
Grapevine *Vitis vinifera*	France All MS	Vinetan	F	Downy mildews: Plasmopara viticola,	Dispersible powder (DP)	8	foliar application spraying	From 1st shoots (BCH10) to cluster tightening (BBCH57) Spring to summer	2 to 6	7 days	1	100 to 300	0.8 to 2.4	1.6 to 14.4	None	The product cannot be applied in rainy period. Apply before or after.

(a): For crops, the EU and Codex classification (both) should be taken into account ; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b): Outdoor or field use (F), greenhouse application (G) or indoor application (I)
(c): e.g. pests as biting and suckling insects, soil born insects, foliar fungi, weeds or plant elicitor
(d): e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR) etc..
(e): GCPF Codes – GIFAP Technical Monograph N° 2, 1989
(f): All abbreviations used must be explained
(g): Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h): Kind, e.g. overall, broadcast, aerial spraying, row, individual plant,
(i): g/kg or g/L. Normally the rate should be given for the active substance (according to ISO)
(j): Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant information on season at time of application
(k): Indicate the minimum and maximum number of application possible under practical conditions of use
(l): The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha
(m): PHI - minimum pre-harvest interval between the plant – type of equipment used must be indicated